

AN 1993:24009176 BIOTECHNO  
 TI Actions of interleukin-4 on prostaglandin biosynthesis at the  
 chorion-decidual interface  
 AU Adamson S.; Edwin S.S.; LaMarche S.; Mitchell M.D.  
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 SO American Journal of Obstetrics and Gynecology, (1993), 169/6 (1442-1447)  
 CODEN: AJOGAH ISSN: 0002-9378  
 DT Journal; Article  
 CY United States  
 LA English  
 SL English  
 AB Objective: We determined the effects of interleukin-4 on chorion and  
 decidual prostaglandin production. Study design: Chorion and decidual  
 cells from term placentas were grown to confluence. Cells were then  
 incubated with interleukin-4 either alone or with other known stimulants  
 of prostaglandin production: interleukin-1 $\beta$ , epidermal growth  
 factor, ionomycin, or phorbol 12-myristate 13-acetate. Prostaglandin  
 E.sub.2 production was determined with a specific radioimmunoassay.  
 Results: Interleukin-4 alone stimulated prostaglandin E.sub.2 production  
 in chorion and decidual cells. Interleukin-4 significantly enhanced the  
 stimulatory actions of phorbol 12-myristate 13-acetate, ionomycin, and  
 epidermal growth factor but not interleukin-1 $\beta$  on prostaglandin  
 E.sub.2 production. Conclusion: Interleukin-4 stimulates prostaglandin  
 E.sub.2 production by chorion and decidual cells. These data suggest that  
 interleukin-4 production by immune effector cells in gestational tissues  
 may contribute to the pathophysiologic features of preterm labor  
 AB. . . data suggest that interleukin-4 production by immune effector cells  
 in gestational tissues may contribute to the pathophysiologic features of  
 preterm labor.  
 CT. . . growth factor; interleukin 1beta; ionomycin; phorbol 13 acetate 12  
 myristate; article; cell culture; controlled study; human; human cell;  
 placenta; premature labor; priority journal; radioimmunoassay;  
 etiology  
 RN (prostaglandin e2) 363-24-6; (epidermal growth factor) 62229-50-9;  
 (ionomycin) 56092-81-0; (phorbol 13 acetate 12 myristate)  
 16561-29-8

AN 1998:226095 BIOSIS  
DN PREV199800226095  
TI Involvement of phosphatidate phosphohydrolase in arachidonic acid mobilization in human amnionic WISH cells.  
AU Balboa, Maria A.; Balsinde, Jesus; Dennis, Edward A. [Reprint author]  
CS Dep. Chem. Biochemistry, Sch. Med., Univ. California San Diego, La Jolla, CA 92093-0601, USA  
SO Journal of Biological Chemistry, (March 27, 1998) Vol. 273, No. 13, pp. 7684-7690. print.  
CODEN: JBCHA3. ISSN: 0021-9258.  
DT Article  
LA English  
ED Entered STN: 20 May 1998  
Last Updated on STN: 20 May 1998  
AB Prostaglandins are known to play a central role in the initiation of labor in humans, and amnionic cells constitute a major source of these compounds. Prostaglandin synthesis and release by amnion cells in response to hormones and ligands takes place after a characteristic 4-5 h lag. However, we report herein that free arachidonic acid (AA), the metabolic precursor of prostaglandins, can be induced at much shorter times (1 h) in human amnionic WISH cells by phorbol 12-myristate 13-acetate (PMA) through activation of protein kinase Calpha (PKCalpha). WISH cells were found to possess both cytosolic group IV phospholipase A2 (cPLA2) and Group VI Ca2+-independent phospholipase A. (iPLA2). Of these, the cPLA2 was found to be the likely mediator of AA mobilization in PMA-activated WISH cells. PMA also activates phospholipase D (PLD) in these cells and ethanol, a compound that inhibits PLD-mediated phosphatidic acid (PA) formation, blocked AA release. Moreover, prevention of PA dephosphorylation by the PA phosphohydrolase inhibitors propranolol and bromoenol lactone, resulted in inhibition of AA release by PMA-treated-WISH cells. Collectively, these data suggest that activation of cPLA2 and attendant AA release by phorbol esters in WISH cells requires prior generation of DAG by phosphatidate phosphohydrolase.  
AB Prostaglandins are known to play a central role in the initiation of labor in humans, and amnionic cells constitute a major source of these compounds. Prostaglandin synthesis and release by amnion cells in.  
RN 506-32-1 (arachidonic acid)  
16561-29-8 (phorbol 12-myristate 13-acetate)  
9025-77-8 (phosphatidate phosphohydrolase)  
9001-84-7 (phospholipase A)  
9001-87-0 (phospholipase D)  
141436-78-4 (PROTEIN KINASE C)

DOCUMENT NUMBER: 1997:457489 HCAPLUS  
127:146000

TITLE: An analysis of the mechanisms involved in the  
okadaic acid-induced contraction of  
the estrogen-primed rat uterus

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Gervaise; Pacaud, Pierre; Candenas, Luz; Molto,  
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Manuel; Martin, Julio D.; Jean-Pierre, Savineau  
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Journal of Pharmacology and Experimental Therapeutics  
(1997), 282(1), 201-207  
CODEN: JPETAB; ISSN: 0022-3565  
Williams & Wilkins

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AB

English

The contractile effect of okadaic acid (OA) and its  
derivs. was investigated in the rat uterus. OA (20  $\mu$ M) induced a  
transient contraction which, after plateauing, slowly decreased. The  
structurally related compound okadanol (20  $\mu$ M) failed to induce any  
significant contraction. Conversely, the synthetic compound Me okadaate (20  
 $\mu$ M) and the naturally occurring ester 7'-hydroxy-4'-methyl-2'-  
methylenhept-4'(E)-enyl okadaate (20  $\mu$ M) were as active as the free  
acid. The OA-induced contraction was unaffected in the presence of  
neomycin (5 mM), mepacrine (30  $\mu$ M), 1-[N,O-bis(1,5-  
isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (10  $\mu$ M),  
calphostin C (3  $\mu$ M) and 1-(5-isoquinolinesulfonyl)-2-methylpiperazine  
(30  $\mu$ M). The calmodulin inhibitor N-(6-aminohexyl)-5-chloro-  
1-naphthalenesulfonamide hydrochloride (100  $\mu$ M) did not modify the  
amplitude of the OA-induced contraction but significantly increased the  
rate of tension decay. The myosin light chain kinase inhibitor  
1-(5-chloronaphthalene-1-sulfonyl)-1H-hexahydro-1,4-diazepine  
hydrochloride (1 mM) significantly reduced the peak amplitude of the  
contraction. Staurosporine (0.03-0.1  $\mu$ M) did not modify the  
contractile component of the OA-induced response but inhibited the  
subsequent decrease in tension. In freshly dispersed myometrial cells  
loaded with the fluorescent  $\text{Ca}^{++}$  indicator indo 1, OA did not produce any  
significant increase in  $[\text{Ca}^{++}]_i$ . OA (5- to 90-min contact) also failed to  
modify the intracellular levels of arachidonic acid, compared with basal  
values. These data suggest that in the rat uterus (1) the  
contractile effect of OA (20  $\mu$ M) is specifically mediated by  
inhibition of protein phosphatases type 1 and/or 2A and is related to a  
direct interaction with the contractile machinery; (2) the decreasing  
phase of the OA-induced mech. response could be mediated by a  
staurosporine-sensitive protein kinase different from protein kinase C.

2003-24475 DRUGU P  
 MEK inhibitor **U0126** delays RU486-induced preterm **labor**  
 in rats.  
 Li Y; Je H; Morgan K G; Malek S  
 Harvard-Med.Sch.; Univ.Boston  
 Boston; Watertown, Mass., USA  
 Anesthesiology (98, Suppl. 1, 11, 2003) 4 Ref.  
 CODEN: ANESAV ISSN: 0003-3022  
 Beth Israel Deaconess Medical Center, Harvard Medical School, Boston,  
 Massachusetts, U.S.A.  
 English  
 Journal  
 AB; LA; CT  
 Literature  
 2003-24475 DRUGU P  
 The effect of the MEK activation inhibitor U-0126 on RU-486-induced  
 pre-term **labor** was investigated in Sprague-Dawley rats. 18-Day  
 pregnant rats were pretreated with U-0126 (100 mg/kg/6 hr, s.c.) and  
**labor** was induced on day 19 with RU-486 (2 mg/kg, s.c.).  
 Treatment with U-0126 delayed the onset of parturition to an average of

25.18 hr after RU-486. Delayed **labor** was associated with  
 activation of ERK2 and phosphorylation of caldesmon in myometrium  
 compared to the sham group. Results suggest that the ERK/caldesmon pathway  
 might be used a target for the development of tocolytics. (conference  
 abstract: Society for Obstetric Anesthesia and Perinatology 35th Annual  
 Meeting, Phoenix, Arizona, USA, May 14-17, 2003). (No EX).

ABEX (E97)  
 TI MEK inhibitor **U0126** delays RU486-induced preterm **labor**  
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 AB The effect of the MEK activation inhibitor U-0126 on RU-486-induced  
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 activation of ERK2 and phosphorylation of caldesmon in myometrium  
 compared to the sham group. Results suggest that the. . .  
 CT [01] U-0126 \*PH; **LABOR** \*OC; DR9800013 \*RN; IN-VIVO \*FT; RAT \*FT;  
 S.C. \*FT; TOCOLYTIC \*FT; CALDESMON \*FT; EC-2.7.1.37 \*FT; LAB.ANIMAL  
 \*FT; INJECTION \*FT; PROTEIN-KINASE. . .